PCT

WORLD INTELLECTUAL PROPE[R]
International Bur[eau]

INTERNATIONAL APPLICATION PUBLISHED UNDER

WO 9608286A1

(51) International Patent Classification 6 : A61M 25/00

A1

(11) International Publication Number: WO 96/08286

(43) International Publication Date: 21 March 1996 (21.03.96)

(21) International Application Number: PCT/US95/10099

(22) International Filing Date: 8 August 1995 (08.08.95)

(30) Priority Data:

08/305,250	13 September 1994 (13.09.94)	US
08/325,958	20 October 1994 (20.10.94)	US

(71) Applicant: LOCALMED, INC. [US/US]; 1820 Embarcadero Road, Palo Alto, CA 94303 (US).

(72) Inventors: ALBA, Paul; 10130 Craft Drive #3, Cupertino, CA 95014 (US). KLEIN, Enrique, J.; 1686 Christina Drive, Los Altos, CA 94024 (US).

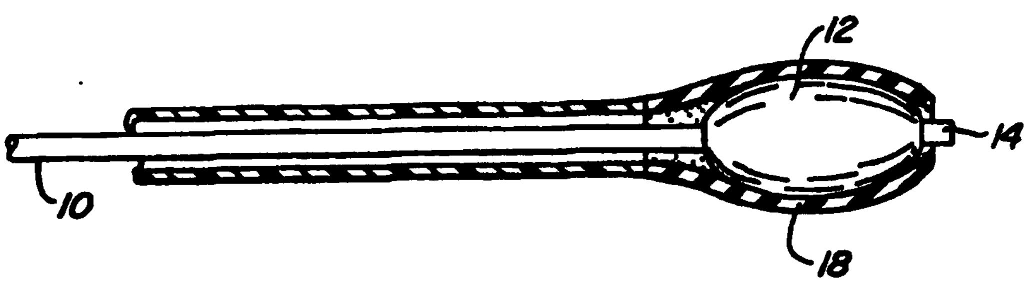
(74) Agents: HANN, James, F. et al.; Townsend and Townsend and Crew, Steuart Street Tower, One Market, San Francisco, CA 94105-1492 (US).

(81) Designated States: AU, CA, JP, European patent (AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE).

Published

With international search report.

(54) Title: CATHETER SLEEVE AND METHOD OF USE



(57) Abstract

A balloon catheter assembly (2) includes a catheter (8) having a catheter shaft (10) with a balloon (12) at its distal end. A sleeve assembly (16) has a diametrically expanding balloon enlargement sleeve (18) at its distal end sized to be positionable over the balloon when the balloon is deflated. The enlargement sleeve can expand from a relaxed condition, at which it is placed over the deflated balloon, to an expanded condition surrounding the fully inflated balloon. The enlargement sleeve is sufficiently thick when expanded for an enlarged dilatation of the vessel when the balloon is reinflated. The enlargement sleeve can be made of elastic or substantially inelastic material; it can also include a porous matrix material with a drug interspersed therein so the drug is applied topically when the vessel is redilated.

FOR THE PURPOSES OF INFORMATION ONLY

Codes used to identify States party to the PCT on the front pages of pamphlets publishing international applications under the PCT.

AT	Austria
AU	Australia
BB	Barbados
BE	Belgium
BF	Burkina Faso
BG	Bulgaria
BJ	Benin
BR	Brazil
BY	Belarus
CA	Canada
CF	Central African Republic
CG	Congo
CH	Switzerland
CI	Côte d'Ivoire
CM	Cameroon
CN	China
CS	Czechoslovakia
CZ	Czech Republic
DE	Germany
DK	Denmark
ES	Spain
FI	Finland
FR	France
GA	Gabon
GB	United Kingdom
GE	Georgia
GN	Guinea
GR	Greece
HU	Hungary
IE	Ireland
IT	Italy
JP	Japan
KE	Kenya
KG	Kyrgystan
KP	Democratic People's Republic of Korea
KR	Republic of Korea
KZ	Kazakhstan
LI	Liechtenstein
LK	Sri Lanka
LU	Luxembourg
LV	Latvia
MC	Monaco
MD	Republic of Moldova
MG	Madagascar
ML	Mali
MN	Mongolia
MR	Mauritania
MW	Malawi
NE	Niger
NL	Netherlands
NO	Norway
NZ	New Zealand
PL	Poland
PT	Portugal
RO	Romania
RU	Russian Federation
SD	Sudan
SE	Sweden
SI	Slovenia
SK	Slovakia
SN	Senegal
TD	Chad
TG	Togo
TJ	Tajikistan
TT	Trinidad and Tobago
UA	Ukraine
US	United States of America
UZ	Uzbekistan
VN	Viet Nam

CATHETER SLEEVE AND METHOD OF USE

CROSS-REFERENCE TO RELATED APPLICATION

This application is a continuation-in-part of application Serial No. 08/222,143, filed April 1, 1994, which was a continuation-in-part of application Serial No. 08/047,737, filed on April 15, 1993, now Patent No. 5,336,178, which was a continuation-in-part of application Serial No. 07/969,595, filed on November 2, 1992, now abandoned, the complete disclosures of which are incorporated herein by reference. This application is also a continuation-in-part of application Serial No. 08/305,250, entitled Perfusion Shunt Device and Method, filed on September 13, 1994, which was a continuation-in-part of application Serial No. 08/221,613, filed on April 1, 1994, the full disclosures of which are incorporated herein by reference. This application is related to Patent No. 5,342,348 and application Serial No. 08/241,428 filed May 11, 1994, the full disclosures of which are incorporated herein by reference.

BACKGROUND OF THE INVENTION

In percutaneous transluminal angioplasty procedures, a catheter having an expansible distal end, usually in the form of a balloon, is positioned in a lumen of a blood vessel with the distal end disposed within a stenotic atherosclerotic region of the vessel. The expansible end is then expanded to dilate the vessel and restore adequate blood flow through the diseased region.

Balloons on conventional angioplasty catheters have low compliance. Therefore, after the balloon is internally pressurized, a further increase of the internal pressure will cause the outside diameter of the balloon to increase only minimally. This prevents the balloon from overexpanding and causing substantial damage to the vessel.

Interventional cardiologists, use on average 1.5 balloon catheters for each procedure. The first catheter used is chosen to have the largest balloon that will cross the stenosis and will also have an inflated diameter of the order of the vessel diameter proximal to the stenosis. Often the diameter of this balloon is smaller than desired in order to cross the lesion. After the first catheter has been expanded, a second catheter is therefore often needed to further dilate the lesion. Typically, the increase in balloon dilatation diameter is 0.5 mm. For example, the first catheter may have a balloon having an expanded diameter of 2.5 mm. In a standard procedure, after the first balloon has been expanded, it is deflated, removed from the patient and a second balloon catheter, typically having a 3.0 mm diameter balloon when expanded, is introduced to the lesion. The balloon is then positioned at the region of stenosis and expanded to its full diameter to further dilate the vessel to the proper size. Since dilatation balloon catheters are designed for single use only and since they are expensive, presently about US $300 to US $800 each, the use of two balloon catheters for each procedure substantially increases the cost of the procedure. Use of two balloon catheters in sequence also increases the length of the procedure.

At times it is desired to deliver a therapeutic agent, typically a drug, to a target site through a body lumen such as an artery, vein or other hollow organs of the gastrointestinal, genitourologic or pulmonary systems. One way to deliver a drug to a target site along the wall of a body passage or lumen is disclosed in U.S. Patent No. 5,304,121 to Sahatjian. It shows a dilatation balloon catheter in which the balloon is coated with a hydrogel polymer layer incorporating a drug in aqueous solution. Upon expansion of the balloon the drug is released to the wall of the body lumen at the target site. This method has its drawbacks and limitations. Hydrogel layers can contain only a limited amount of drug and the drug tends to diffuse quickly out of the hydrogel where it is subject to being washed away by the blood stream prior to reaching the target site. Both

of these factors can limit the effectiveness of using a hydrogel layer to deliver a drug to a target site.

SUMMARY OF THE INVENTION

This invention relates generally to intravascular dilatation devices, and more specifically to an intravascular sleeve catheter which eliminates the need for the use of a second balloon catheter, where such a second catheter expands to a larger diameter than the first, to definitively dilate a vessel.

The present invention is directed to a balloon catheter assembly and its method of use. The catheter assembly includes a dilatation balloon catheter having a catheter shaft with a balloon at the distal end of the catheter shaft. A sleeve assembly has a radially expanding enlargement sleeve at its distal end sized to be positionable over the balloon of the dilatation catheter when the balloon is in the deflated condition. The enlargement sleeve can expand from a pre-use, relaxed condition, at which it is placed over the deflated balloon, to an in-use, expanded condition surrounding the fully inflated balloon. The enlargement sleeve when in the expanded or in-use condition has a radial thickness sufficient to enhance or enlarge the dilatation of the vessel at the site of the lesion when the balloon of the dilatation catheter is reinflated.

A primary advantage of the invention is that it eliminates the need for using a second costly balloon dilatation catheter to achieve the necessary enlargement of a vessel. The sleeve catheter is simpler in construction and should be much less expensive than a second standard balloon dilatation catheter so that significant monetary savings can be achieved. Also, since replacement or exchange of balloon dilatation catheters is not necessary, the entire procedure can be done more quickly which also represents a cost savings; the balloon from the first and only dilatation catheter is inflated to dilate the target site and then deflated, after which the balloon enlargement sleeve, which can be pre-loaded over the shaft of the dilatation or angioplasty catheter, is

aligned over the deflated balloon and the balloon is reinflated so as to expand the target site to the enlarged diameter determined by the inflated diameter of the balloon, which remains the same in both cases, plus twice the radial thickness of the enlargement sleeve. This can increase the speed and lower the cost of the procedure over that of a conventional procedure using two separate balloon dilatation catheters sequentially.

The axial stiffness of the enlargement sleeve necessary to permit it to advance through the lumen and over the dilatation balloon to the target site is preferably provided by one or more axially extending stiffener elements. The stiffener elements preferably have a flattened rectangular cross-sectional shape and are embedded within the wall of the enlargement sleeve. Radiopaque markers can be incorporated into the stiffener elements to assist with the proper alignment of the enlargement sleeve over the balloon of the dilatation catheter.

The enlargement sleeve can be made of an elastomeric or of a substantially inelastic material. In one embodiment the enlargement sleeve is of an elastomeric material, the relaxed thickness of which is chosen so that when aligned with the inflated balloon, the radial thickness of the elastic enlargement sleeve is sufficient to incrementally dilate the vessel. In another embodiment the enlargement sleeve is made of a substantially inelastic material made radially expandable by virtue of a series of slits or other separations which permit the enlargement sleeve to expand radially as the balloon expands. With this type, the thickness of the wall of the enlargement sleeve remains substantially constant and is chosen to provide the additional thickness desired during the re-expansion of the balloon.

Another aspect of the invention is the use of a porous matrix material containing a drug interspersed therein in at least a portion of the region of expansion of the enlargement sleeve. This enables the enlargement sleeve to administer a drug to the target site when the balloon is expanded. An advantage of this aspect of the invention is

that no separate drug delivery lumen is needed. Another advantage results from the fact that the enlargement sleeve can be made substantially thicker than the thickness of a hydrogel layer, a conventional method for delivering a drug to a target site. While a hydrogel layer may be on the order of 0.05 mm thick, the enlargement sleeve can be made substantially thicker and even after being expanded over an angioplasty balloon, can be typically from 0.25 to 0.50 mm thick. This is possible since the relaxed thickness of the enlargement sleeve affects the introducing profile of the dilatation balloon only after the original dilatation has taken place, leaving a substantially larger vessel lumen for the reintroduction of the combination dilatation balloon and sleeve. The thicker porous matrix material, which is typically made from an elastomeric material, can be made to absorb or carry substantially more drug usually up to 100 times more than the 10 to 30 milligrams of drug usually carried by a conventional hydrogel layer. Also, drug in a hydrogel layer is subject to being substantially washed away by the flow of blood around this hydrogel layer prior to dilatation. The drug in the porous matrix material may be retained better than in the hydrogel layer because the bulk of the drug is well below the surface of the matrix, and the porous matrix can be engineered to have smaller pores on its outer surface. Other losses of the drug in the porous matrix material, typically through a decrease in the thickness of the porous matrix material during expansion of the balloon can be minimized by providing longitudinal slits in the porous matrix and sealing off the walls of the slits, or, the drug interspersed within the porous matrix material can be contained in microcapsules which rupture and release the drug only when the porous matrix comes in contact with the vessel wall and the balloon applies additional pressure on the constrained porous matrix. Additionally, bioabsorbable particles comprising drugs dispersed in polyglycolic/ polylactic acid matrices can be distributed within the porous matrix. When the balloon is inflated and the porous matrix sleeve becomes squeezed between the balloon and the inner

surface of the body lumen, these granules will be forced into the tissue at the target site.

Other features and advantages of the invention will appear from the following description in which the preferred embodiments have been discussed in detail in conjunction with the accompanying drawings.

BRIEF DESCRIPTION OF THE DRAWINGS

Fig. 1 is a simplified side view showing a catheter assembly including a dilatation balloon catheter and an elastomeric enlargement sleeve with the dilatation balloon positioned at a region of stenosis within a blood vessel prior to inflation of the balloon;

Figs. 1A, 1B and 1C show the balloon catheter assembly of Fig. 1 with the balloon inflated in Fig. 1A, with the balloon deflated and the relaxed enlargement sleeve advanced to a distal position overlying the balloon in Fig. 1B, and with the balloon inflated and enlargement sleeve expanded so the thickness of the enlargement sleeve provides an additional radial expansion of the region of stenosis resulting in a two-stage dilatation of the region;

Fig. 2 is an enlarged view of the distal end of an enlargement sleeve assembly with a substantially inelastic enlargement sleeve in a relaxed condition illustrating longitudinal stiffener elements and radially extending slits in the enlargement sleeve;

Fig. 2A illustrates the enlargement sleeve of Fig. 2 having the catheter shaft therein and the dilatation balloon inflated so as to place the enlargement sleeve in its expanded condition similarly to Fig. 1C;

Fig. 2B is a cross-sectional view taken along line 2B-2B of Fig. 2A with the addition of a vessel being dilated over the enlargement sleeve;

Fig. 3 shows a cross-sectional view of an elastomeric enlargement sleeve in a relaxed condition;

Fig. 3A illustrates the enlargement sleeve of Fig. 3 in an expanded condition showing how the wall thickness decreases during expansion; and

Fig. 4 is a partial side view of an alternative embodiment of the sleeve assembly of Fig. 1.

DESCRIPTION OF A FIRST PREFERRED EMBODIMENT

Fig. 1 illustrates, in simplified form, a catheter assembly 2 showing the distal end within a blood vessel 4. Assembly 2 includes a proximal end fitting 6 through which a dilatation balloon catheter 8 passes. Balloon catheter 8 includes a catheter shaft 10 and a dilatation balloon 12 at the distal end 14 of catheter shaft 10. A guide wire 15 is used within catheter shaft 10.

A tubular sleeve assembly 16 is slidably mounted over catheter shaft 10. In the embodiment of Fig. 1, sleeve assembly 16 includes tubular, radially expandable, elastomeric enlargement sleeve 18 at the distal end of sleeve assembly 16 and a connecting tube 20 coupling enlargement sleeve 18 to proximal end fitting 6. The thickness of enlargement sleeve 18 is exaggerated in Figs. 1A-1C. Movement of fitting 6 from the solid line position to the dashed line position of Fig. 1 causes enlargement sleeve 18 to move from the position of Fig. 1 to the position of Fig. 1B as discussed below.

In a first preferred embodiment, dilatation balloon catheter 8 is of a conventional design having a low compliance dilatation balloon 12. Tubular sleeve assembly 16 could be made from an elastomeric material, such as a medical grade synthetic rubber, Santoprene® (Advanced Elastomeric Systems) or a thermoplastic elastomeric polyurethane sold under the trademark Tecoflex® by Thermedics, Inc. or Kraton® by Shell Chemical Co. However, the radially expandable enlargement sleeve 18 is preferably fabricated as a separate component, including its own axially extending stiffeners, and then thermally, mechanically or otherwise bonded to a connecting tube 20 using conventional methods; connecting tube 20 would preferably be made of a conventional biocompatible, relatively inelastic but flexible material, such as Pebax®, polyester or polyethylene. The joint between enlargement sleeve 18 and its associated connecting tube, not shown, can be made in a variety of ways, such as by overlapping inner and outer

portions of the sleeve and connecting tube to create a good joint using adhesives, should thermal bonding prove impractical.

To provide appropriate longitudinal stiffness for enlargement sleeve 18 so it may be maneuvered into position over dilatation balloon 12 without collapsing, axially extending stiffeners 26, see Fig. 2, are incorporated into enlargement sleeve 18. Stiffeners 26 are preferably made of stainless steel but can also be made of a superlastic nickel titanium alloy called Nitinol, and are approximately 40 mm long, with a rectangular cross section to fit within the wall of the enlargement sleeve. Alternatively, they may also be made with round, elliptical, oval or other cross sectional shapes. Stiffeners 26 will typically extend into connecting tube 20 about 5-10mm. It is preferable that stiffener elements 26 used with enlargement sleeve 18 extend across the joint between the enlargement sleeve and the connecting tube to improve the joint strength.

To assist proper axial alignment of enlargement sleeve 18 with balloon 12, radiopaque markers may be provided on the distal portion of catheter assembly 2. Preferably radiopaque markers are disposed on one or more of stiffeners 26. Markers are formed by, for example, plating a radiopaque material such as gold or platinum onto stiffeners 26. Dilatation balloon catheter 8 will also have a radiopaque marker typically in the form of a gold or platinum band on catheter shaft 10 adjacent balloon 12. In one embodiment, two markers are disposed on at least one stiffener 26, the markers being separated a distance from one another usually about equal to or slightly greater than the length of the marker on catheter shaft 10. In this way, by visualization through radiographic imaging, the markers on stiffener 26 facilitate axial alignment of enlargement sleeve 18 with balloon 12 by aligning the marker on catheter shaft 10 between the markers on stiffeners 26. The markers further provide visual indication of the location of balloon 12 within vessel 4 so that balloon 12 may be positioned adjacent to a treatment site. Other arrangements of radiopaque markers can be used as

well, such as disclosed in U.S. Patent No. 5,336,178 and in co-pending application Serial No. 08/241,428.

Figs. 1A-1C illustrate the distal portion of catheter assembly 2 in simplified form during its use. Fig. 1A shows catheter assembly 2 in the same position as shown in Fig. 1 but with balloon 12 expanded to dilate target area 28 at the region of stenosis. After dilatation balloon 12 is deflated, proximal end fitting 6 is moved from the solid line position to the dashed line position of Fig. 1. This drives enlargement sleeve 18 over the deflated dilatation balloon 12 as shown in Fig. 1B. Dilatation balloon 12 is then re-expanded, thus expanding enlargement sleeves 18 or 18a as shown in Figs. 1C and 2A. The diameter of dilatation balloon 12 is the same in Figs. 1A and 1C. However, the effective diameter of catheter assembly 2 at target area 28 is increased by the expanded thickness of elastomeric enlargement sleeve 18 or the substantially constant thickness of enlargement sleeve 18a. This permits the incremental enlargement of a region of stenosis 28 by a known predetermined value. This also eliminates the need to remove balloon catheter 8 after expanding balloon 12 and replacing balloon catheter 8 with another balloon catheter having a dilatation balloon which expands to a larger diameter. The present invention not only saves time, it can also save money since sleeve assembly 16 should be less expensive to manufacture than a balloon catheter 8.

It is clear that when the expandable enlargement sleeve 18 is made of an elastomeric material, the initial relaxed wall thickness of this sleeve will decrease as it is expanded by the underlying balloon 12 of the dilatation balloon catheter 8.

Fig. 3 illustrates a cross-sectional view showing an elastomeric enlargement sleeve 18b in a relaxed state. As shown in Fig. 3, in this state enlargement sleeve 18b has an outside diameter D_1, and an inside diameter d_1 and a wall thickness t_1. Upon expansion as shown in Fig. 3A, the outside diameter, the inside diameter and the wall thickness for enlargement sleeve 18b are labelled D_2, d_2 and t_2

respectively. Assuming that longitudinal contraction of the enlargement sleeve is minimal during expansion, the cross-sectional area will remain essentially constant. For known values of d_1, d_2 and a desired wall thickness t_2, an algebraic expression for the initial wall thickness t_1 can be derived as:

$$t_1 = \frac{-d_1}{2} \pm \sqrt{\left(\frac{d_1}{2}\right)^2 + t_2(t_2+d_2)}$$

As an example, assuming t_2 equals 0.25 mm and d_1 equals 1.27 mm (0.05 inch), the following values of t_1 are obtained as a function of d_2: when d_2 equals 2.0, 2.5, 3.0 and 3.5 mm, t_1 equals 0.35, 0.41, 0.47 and 0.52 mm, respectively.

The inside surface 23 of elastomeric enlargement sleeve 18 is a lubricous surface to help sleeve 18 slide onto and off of balloon 12. The outside surface of elastomeric sleeve 18 is also lubricious.

Sleeve 18 is preferably made so that it has a uniform thickness when in its relaxed condition of Figs. 1, 1A and 1B, and a uniform, although reduced, thickness when in the expanded condition of Fig. 1C. To exhibit a uniform radial thickness when sleeve 18 is in the expanded condition, the sleeve thickness should not vary more than about ± 10% from the average thickness.

Fig. 4 illustrates an alternative embodiment of the sleeve assembly 16 of Fig. 1. Sleeve assembly 16a is like sleeve assembly 16 but instead of using a connecting tube 20, which surrounds catheter shaft 10, a connecting rod 20a, which lies parallel to but does not surround shaft 10, is used. Rod 20a can be solid, hollow, or of other construction.

The wall thickness of enlargement sleeve 18 for intravascular use is preferably about 0.25 to 0.50mm when expanded. Depending on the balloon size used, this will typically provide a diametral expansion in the range of 110 to 140%.

In use, balloon catheter 8 is positioned with dilatation balloon 12 deflated at target area 28, typically a

region of stenosis. This is usually accomplished with the aid of a guide wire 15, as is conventional. While sleeve assembly 16 could be placed into the position of Figs. 1 and 1A after balloon catheter 8 alone has been deployed and then withdrawn from the patient's body, sleeve assembly 16 is preferably inserted into blood vessel 4 along with the initial placement of balloon catheter 8 within the blood vessel. Balloon 12 is then inflated to dilate region of stenosis 28 as suggested in Fig. 1A. Balloon 12 is then deflated and proximal end fitting 6 is moved from the solid line position to the dashed line position of Fig. 1 to move enlargement sleeve 18 over dilatation balloon 12 as suggested in Fig. 1B. However, catheter shaft 10 could also be pulled proximally to position deflated dilatation balloon 12 within enlargement sleeve 18; both balloon 12 and sleeve 18 would then be pushed distally into position at the region of stenosis 28. In either event, balloon 12 is then reinflated to the condition of Fig. 1C with enlargement sleeve 18 surrounding the dilatation balloon so as to provide an additional enlargement at, and optionally apply a drug to target area 28 as later described in a third preferred embodiment.

Sometimes it may not be necessary to follow all the steps above when target area 28 does not require the two-step dilatation procedure of Figs. 1-1C. In such case, the user could, for example, position deflated dilatation balloon 12 at the target area 28 as shown in Fig. 1, move enlargement sleeve 18 over the deflated dilatation balloon and then inflate the dilatation balloon to the condition of Fig. 1C. This may prove especially useful when applying a drug to target area 28 as preventive therapy.

DESCRIPTION OF A SECOND PREFERRED EMBODIMENT

Enlargement sleeve 18a, see Figs. 2-2B, is created from an extension of connecting tube 20 and has a pattern of axially extending slits 24 which permit enlargement sleeve 18a to expand radially when dilatation balloon 12 is inflated with the enlargement sleeve positioned over the dilatation balloon. The radial thickness of enlargement sleeve 18a is preferably

about 0.25 mm and may be of a different thickness than that of connecting tube 20. For a 20mm long balloon, enlargement sleeve 18 is about 30mm long and has a number of offset slits 24 to permit sleeve 18 to expand radially over balloon 12 as shown in Fig. 2A.

In Fig. 2B a vessel 30 is shown in cross section being distended by enlargement sleeve 18 and underlying balloon 12 of dilatation balloon catheter 8. The cross section is taken at line 2B-2B in Fig. 2A. To maximize the dilatation effect of enlargement sleeve 18, a larger, rather than a smaller, number of offset slits 24 is desirable since the remaining webs 32 between slits 24 act as supports for the vessel tissue, which tends to span the gaps between the webs in an essentially straight manner. The number of offset slits 24, their geometrical arrangement and their length determine the range of expansibility of enlargement sleeve 18. When such an enlargement sleeve is expanded over a dilatation balloon catheter, the free webs of the enlargement sleeve tend to twist around their own axes. This tendency is not apparent when in use since the free webs are compressively contained between balloon 12 and the tissue of vessel 30.

With sleeve assembly 16, of this second preferred embodiment, the entire sleeve assembly is preferably made of the same material as connecting tube 20. This can eliminate the need for special joining techniques.

DESCRIPTION OF A THIRD PREFERRED EMBODIMENT

Another important aspect of the invention involves the use of a modified elastomeric enlargement sleeve having a porous matrix material containing a drug interspersed therein. Porous matrix materials are materials which have pores, voids or other interconnected openings or regions which can contain other materials, such as liquids, gels, microcapsules or granules. Biocompatible microporous polymeric materials having interconnecting pores of controlled pore size in the range of 0.1 to 100 or more microns, and pore size gradients throughout their thicknesses, have been manufactured both in sheet and tubular form. Examples of these porous matrix materials

include Mitraflex™ and Spyroflex™, both tradenames of PolyMedica, Woburn, MA., which are modified polyurethane formulations manufactured by a liquid extrusion process also involving a phase separation utilizing controlled coagulation techniques. (See U.S. Patent Nos. 4,704,130 and 4,813,966 incorporated herein by reference.) These materials have already found use in the field of wound dressings and are being tested in the field of vascular grafts.

The drug to be interspersed within the porous matrix material can be in the form of an aqueous solution, or, an aqueous solution contained within microcapsules, or, solid bioabsorbable particles. Microcapsules can be rupturable when externally pressurized. Bioabsorbable particles can be embedded in the vessel tissue by the balloon acting against the catheter sleeve as explained later.

It should be understood that the catheter of the present invention is suitable for delivery of a variety of therapeutic agents including pharmaceuticals, proteins, peptides, nucleotides, carbohydrates, polysaccharides, muccopolysaccharides, simple sugars, glycosaminoglycans and steroids. The present invention facilitates delivery of such agents in a variety of formulations, including aqueous vehicle or liposome. The catheter is further useful for the delivery of viral particles to facilitate gene transfer. The agents delivered may perform in a variety of functions, including antithrombotics, antiplatelets, antimetabolics, growth factor inhibitors, growth promoters, anticoagulants, antimitotics, and antibiotics.

This third preferred embodiment may be constructed either in the form of a continuous porous elastomeric sleeve 18 as shown in Figs. 1-2C or a porous elastomeric sleeve 18a with slits as shown in Figs. 2-2B. Figs. 2-2B will be used in describing the slit version of the third embodiment. The technique for cutting the slits would typically involve sealing off the surfaces 36 of the porous matrix material on both sides of the slit. Such a sealing process can be achieved through the use of a heated blade or laser cutting technology. A sealing process would also be used on the inner

lumen of sleeve 18a. The drug is preferably introduced to the porous matrix following the final catheter assembly, which includes the slitting and sealing operations. The purpose of providing slits with sealed side surfaces 36 is to minimize the loss of drug during the expansion of enlargement sleeve 18a prior to reaching the interior wall of the vessel in the manner illustrated in Fig. 2B. It will be appreciated that the webs 32 of the porous matrix material will distend and thin out when expanded in the manner of sleeve 18 of Figs. 2A and 2B due to the elastomeric nature of the material, but not to the same extent as if the sleeve had been kept unslit. This small distension, combined with the sealed inner luminal surfaces 38 and the sealed side surfaces 36 of slits 24, will provide for some, but nevertheless minimal release of drug from the porous matrix material through the surface of sleeve 18a during the expansion of the enlargement sleeve. As the enlargement sleeve 18a is further expanded to contact vessel 30 as shown in Fig. 2B and is squeezed between balloon 12 and the vessel wall, the drug in the porous matrix material is then forced through the outer surface 40 of sleeve 18a and into the tissue of the vessel wall providing the desired therapeutic benefit.

Since the drug is captured within the porous matrix material and not on its outer surface 40, the possibility of a drug washout in the blood stream is minimized.

In the case of the drug being carried in microcapsules within the porous matrix material of an expansion sleeve 18a, the expansion of balloon 12 and the squeezing of the porous matrix material against the inner vessel wall can create sufficient pressure to rupture the microcapsules to allow the contents to be released and forced into the vessel wall.

When the drug is in the form of bioabsorbable particles housed in the porous matrix material, as the porous matrix material of sleeve 18a is squeezed between the expansion balloon 12 and the inner vessel wall, and since the balloon surface is a tough impermeable membrane, the bioabsorbable particles will be forced into the softer vessel

tissue where they will become embedded in readiness for their pre-programmed, time release of therapeutic drug.

Other modifications and variation can be made to the disclosed embodiments and methods without departing from the subject of the invention as defined in the following claims. For example, an enlargement sleeve including both an elastomeric, or other elastic material with or without drugs interspersed therein, and a substantially inelastic portion can be used.

<u>WHAT IS CLAIMED IS</u>:

1. A method for using a balloon catheter comprising the following steps:

inserting a balloon catheter, of the type including a balloon, into a body lumen;

aligning the balloon with a target site;

inflating the balloon to dilate the target site to a first diametral dimension;

deflating the balloon;

selecting an expandable balloon enlargement sleeve;

positioning the balloon enlargement sleeve in alignment with the deflated balloon at the target site; and

reinflating the balloon so as to expand the enlargement sleeve therewith at the target site to dilate the target site to a second diametral dimension.

2. The method of claim 1 wherein the inserting step is carried out within the lumen of a blood vessel.

3. The method of claim 1 wherein the selecting step includes the step of selecting an elastic enlargement sleeve.

4. The method of claim 1 wherein the selecting step includes the step of selecting an effectively inelastic enlargement sleeve.

5. The method of claim 1 wherein the inserting step is carried out by simultaneously inserting both the balloon catheter and the balloon enlargement sleeve therewith into the body lumen.

6. The method of claim 5 wherein the simultaneously inserting step is carried out with the balloon distal to the enlargement sleeve.

7. The method of claim 5 wherein the simultaneously inserting step is carried out with the balloon aligned with the enlargement sleeve.

8. The method of claim 1 wherein the positioning step is carried out by moving the enlargement sleeve relative to the balloon catheter.

9. The method of claim 1 further comprising the step of moving the deflated balloon from the target site and wherein the positioning step includes the steps of aligning the enlargement sleeve and the deflated balloon and then moving said aligned enlargement sleeve and deflated balloon to the target site.

10. The method of claim 8 wherein the moving step is carried out while maintaining the balloon at the target site.

11. The method of claim 1 further comprising the step of sizing the enlargement sleeve so that the second diametral dimension is greater than the first diametral dimension by a predetermined amount.

12. The method of claim 1 wherein the selecting step includes the step of selecting an enlargement sleeve having a wall thickness sufficient to make the second diametral dimension at least about 110% of the first diametral dimension.

13. The method of claim 1 wherein the selecting step includes the step of selecting an enlargement sleeve having a wall thickness of about 0.25 to 0.50mm when expanded.

14. The method of claim 1 wherein the selecting step includes the step of selecting an enlargement sleeve having numerous axial openings formed therein to facilitate diametral expansion of the enlargement sleeve.

15. The method of claim 1 wherein the selecting step includes the step of selecting an enlargement sleeve made of an elastomeric material.

16. The method of claim 1 wherein the selecting step includes the step of selecting an enlargement sleeve made of a flexible but effectively inelastic material.

17. The method of claim 1 wherein the selecting step includes the step of selecting an enlargement sleeve having a distal portion surrounding the balloon catheter and a proximal portion.

18. The method of claim 11 wherein the positioning step includes the step of manipulating the distal portion using a push rod as the proximal portion.

19. The method of claim 1 wherein the selecting step includes the step of selecting an enlargement sleeve made of a lubricious material.

20. The method of claim 1 further comprising the step of positioning the balloon and the enlargement sleeve relative to one another using radiopaque markers.

21. The method of claim 1 further comprising the step of predicting the second diametral dimension based upon the first diametral dimension and the enlargement sleeve selected.

22. The method of claim 21 wherein the predicting step includes the step of determining if the enlargement sleeve is made of an elastomeric material and, if so, predetermining an expected reduction in the thickness of the elastomeric material when the balloon is reinflated.

23. A method for using a balloon catheter comprising the following steps:

inserting a balloon catheter, of the type including a balloon, into a body lumen;

aligning the balloon with a target site;

inflating the balloon to dilate the target site to a first diametral dimension;

deflating the balloon;

selecting an expandable balloon enlargement sleeve at least a portion of which is made of a porous matrix material containing a drug interspersed therein;

positioning the balloon enlargement sleeve in alignment with the deflated balloon at the target site; and

reinflating the balloon so as to expand the enlargement sleeve therewith at the target site to squeeze the expanded enlargement sleeve against the inner surface of the body lumen thereby administering said drug to the target site from the porous matrix material.

24. The method of claim 23 further comprising the step of selecting a porous matrix material having axially extending openings to facilitate diametral expansion of the enlargement sleeve.

25. The method of claim 24 further comprising the step of selecting an enlargement sleeve in which the openings are defined by sealed surfaces.

26. The method of claim 23 further comprising the step of selecting an elastomeric material as the porous matrix material.

27. A method for using a balloon catheter comprising the following steps:

selecting a drug;

selecting an expandable sleeve at least a portion of which is made of a porous matrix material containing said drug interspersed therein;

inserting a balloon catheter, of the type including a balloon, into a body lumen;

positioning the sleeve in alignment with the deflated balloon at the target site; and

inflating the balloon so as to expand the sleeve therewith at the target site to squeeze the expanded sleeve against the inner surface of the body lumen thereby administering said drug to the target site from the porous matrix material.

28. The method of claim 27 further comprising the step of selecting a biocompatible microporous polymeric material having interconnecting pores as the porous matrix material.

29. The method of claim 27 wherein the drug selecting step includes the step of selecting the drug interspersed in the porous matrix material in fluid form.

30. The method of claim 27 wherein the drug selecting step includes the step of selecting the drug interspersed in the porous matrix material in microencapsulated form.

31. The method of claim 27 wherein the drug selecting step includes the step of selecting the drug interspersed in the porous matrix material in microcapsules that rupture under pressure.

32. The method of claim 27 wherein the drug selecting step includes the step of selecting the drug interspersed in the porous matrix material in the form of bioabsorbable elements.

33. The method of claim 32 wherein the drug selecting step includes the step of selecting bioabsorbable elements having at least one of either polyglycolic or polylactic acid drug matrices in granular form for distribution within the porous matrix material.

34. The method of claim 32 further comprising the step of forcing the bioabsorbable elements into the target site tissue upon squeezing the porous matrix material against the inner surface of the body lumen.

35. The method of claim 27 comprising the step of positioning the balloon and the enlargement sleeve relative to one another using radiopaque markers.

36. The method of claim 27 further comprising the step of predicting a reduction in thickness of the expandable sleeve when the balloon is inflated and the sleeve is expanded.

37. A catheter assembly comprising:

a balloon catheter including a catheter shaft having proximal and distal ends and a balloon at the distal end of the catheter shaft, the balloon placeable into inflated and deflated conditions, the balloon having inflated and deflated diametral dimensions corresponding to the inflated and deflated conditions;

a sleeve assembly, having proximal and distal ends, comprising an expansible enlargement sleeve at the distal end sized to be positionable over the balloon when the balloon is in the deflated condition; and

the enlargement sleeve having a radial thicknesses when the enlargement sleeve is in a distal position over the balloon and the balloon is in the inflated condition so as to place the enlargement sleeve in an expanded condition, said radial thicknesses adding significantly to the inflated balloon diametral dimension.

38. The assembly of claim 37 wherein the sleeve assembly includes a connecting portion.

39. The assembly of claim 38 wherein the connecting portion includes a tubular connecting portion surrounding the catheter shaft.

40. The assembly of claim 38 wherein the connecting portion includes a connecting rod generally parallel to but radially offset from the catheter shaft.

41. The assembly of claim 37 wherein the sleeve assembly includes at least one axial stiffener element.

42. The assembly of claim 37 wherein the enlargement sleeve includes axially extending openings to facilitate radial expansion.

43. The assembly of claim 42 wherein the enlargement sleeve is made of a flexible but effectively inelastic material.

44. The assembly of claim 37 wherein the enlargement sleeve is made of an elastomeric material.

45. The assembly of claim 37 wherein the enlargement sleeve has an inner surface, said inner surface being lubricious.

46. The assembly of claim 37 wherein the radial thicknesses of the enlargement sleeve add at least about 10% to the effective diametral dimension of the balloon when the enlargement sleeve is in the use condition.

47. The assembly of claim 37 wherein a single radial wall thickness of the enlargement sleeve is about 0.25 to 0.50mm when the enlargement sleeve is in the use condition.

48. The assembly of claim 47 wherein a single radial thickness of the enlargement sleeve when in the expanded condition does not vary more than about ± 10% from an average radial thickness of the enlargement sleeve.

49. A catheter sleeve assembly, for use with a balloon catheter of the type having a balloon placeable in inflated and deflated conditions, comprising:

proximal and distal ends;

an expansible enlargement sleeve at the distal end sized to be positionable over the balloon when the balloon is in the deflated condition; and

the enlargement sleeve having a uniform radial thickness when the enlargement sleeve is in a distal position in alignment over the balloon and the balloon is in the inflated condition so as to place the enlargement sleeve in an expanded condition, said radial thickness being a significant fraction of the inflated balloon diametral dimension.

50. The assembly of claim 49 wherein the sleeve assembly includes a connecting portion.

51. The assembly of claim 50 wherein the connecting portion includes a tubular connecting portion surrounding the catheter shaft.

52. The assembly of claim 50 wherein the connecting portion includes a connection rod generally parallel to but radially offset from the catheter shaft.

53. The assembly of claim 49 wherein the sleeve assembly includes at least one axial stiffener element.

54. The assembly of claim 49 wherein the enlargement sleeve includes axially extending openings to facilitate radial expansion.

55. The assembly of claim 54 wherein the enlargement sleeve is made of a flexible but effectively inelastic material.

56. The assembly of claim 49 wherein the enlargement sleeve is made of an elastomeric material.

57. The assembly of claim 49 wherein the enlargement sleeve has an inner surface, said inner surface being lubricous.

58. The assembly of claim 49 wherein the radial thicknesses of the enlargement sleeve add at least about 10% to the effective diametral dimension of the balloon when the enlargement sleeve is in the use condition.

59. The assembly of claim 49 wherein a single radial wall thickness of the enlargement sleeve is about 0.25 to 0.50mm when the enlargement sleeve is in the use condition.

60. The assembly of claim 59 wherein a single radial thickness of the enlargement sleeve when in the expanded condition does not vary more than about ± 10% from an average thickness of the enlargement sleeve.

61. A catheter assembly, for use in a body lumen, comprising:

a balloon catheter including a catheter shaft having proximal and distal ends and a balloon at the distal end of the catheter shaft, the balloon placeable into inflated and deflated conditions, the balloon having inflated and deflated diametral dimensions corresponding to the inflated and deflated conditions;

a sleeve assembly, having proximal and distal ends, comprising a diametrically expandable enlargement sleeve at the distal end sized to be positionable over the balloon when the balloon is in the deflated condition; and

at least a portion of the enlargement sleeve comprising a porous matrix material containing a drug interspersed therein, the enlargement sleeve having an outer surface through which the drug can be dispensed when the enlargement sleeve is in a distal position over the balloon and the balloon is in the inflated condition so as to squeeze the enlargement sleeve in an expanded condition against an

inner surface of the body lumen thereby administering said drug to a target site from the porous matrix material.

62. The assembly of claim 61 wherein the porous matrix material is made from a biocompatible microporous polymeric material having interconnecting pores.

63. The assembly of claim 61 wherein the drug is in liquid form within the porous matrix material.

64. The assembly of claim 61 wherein the drug is in encapsulated microcapsules.

65. The assembly of claim 61 wherein the drug is in the form of bioabsorbable elements.

66. The assembly of claim 64 wherein the microcapsules can rupture under pressure so the microcapsules release the drug into the target site tissue upon compressing the capsules in the squeezed porous matrix material.

67. The assembly of claim 64 wherein the microcapsules have bioabsorbable shells so the microcapsules release the drug into a patient's tissue after the microcapsules have been forced into said tissue through the outer surface of said porous matrix material.

68. The assembly of claim 65 wherein the bioabsorbable elements comprise drugs dispersed in at least one of either polyglycolic or polylactic acid drug matrices in granular form distributed within the porous matrix material.

69. The assembly of claim 68 wherein the bioabsorbable elements are forced into the target site tissue upon squeezing the porous matrix material against the inner surface of the body lumen.

70. A catheter sleeve assembly, for use in a body lumen, comprising:

proximal and distal ends;

a diametrically expandable enlargement sleeve at the distal end; and

at least a portion of the enlargement sleeve comprising a porous matrix material containing a drug interspersed therein, the enlargement sleeve having an outer surface through which the drug can be dispensed when the enlargement sleeve is compressed against a body surface thereby administering said drug to a target site from the porous matrix material.

71. The assembly of claim 70 wherein the porous matrix material is made from a biocompatable microporous polymeric material having interconnecting pores.

72. The assembly of claim 70 wherein the drug is in liquid form within the porous matrix material.

73. The assembly of claim 70 wherein the drug is encapsulated in microcapsules.

74. The assembly of claim 70 wherein the drug is in the form of bioabsorbable elements.

75. The assembly of claim 73 wherein the microcapsules can rupture under pressure so the microcapsules release the drug into the target site tissue upon compressing the capsules in the compressed porous matrix material.

76. The assembly of claim 73 wherein the microcapsules have bioabsorbable shells so the microcapsules release the drug into a patient's tissue after the microcapsules have been forced into said tissue through the outer surface of said porous matrix material.

77. The assembly of claim 74 wherein the bioabsorbable elements comprise drugs dispersed in at least one of either polyglycolic or polylactic acid drug matrices in granular form distributed within the porous matrix material.

78. The assembly of claim 77 wherein the bioabsorbable elements are forced into the target site tissue upon compressing the porous matrix material against the body surface.

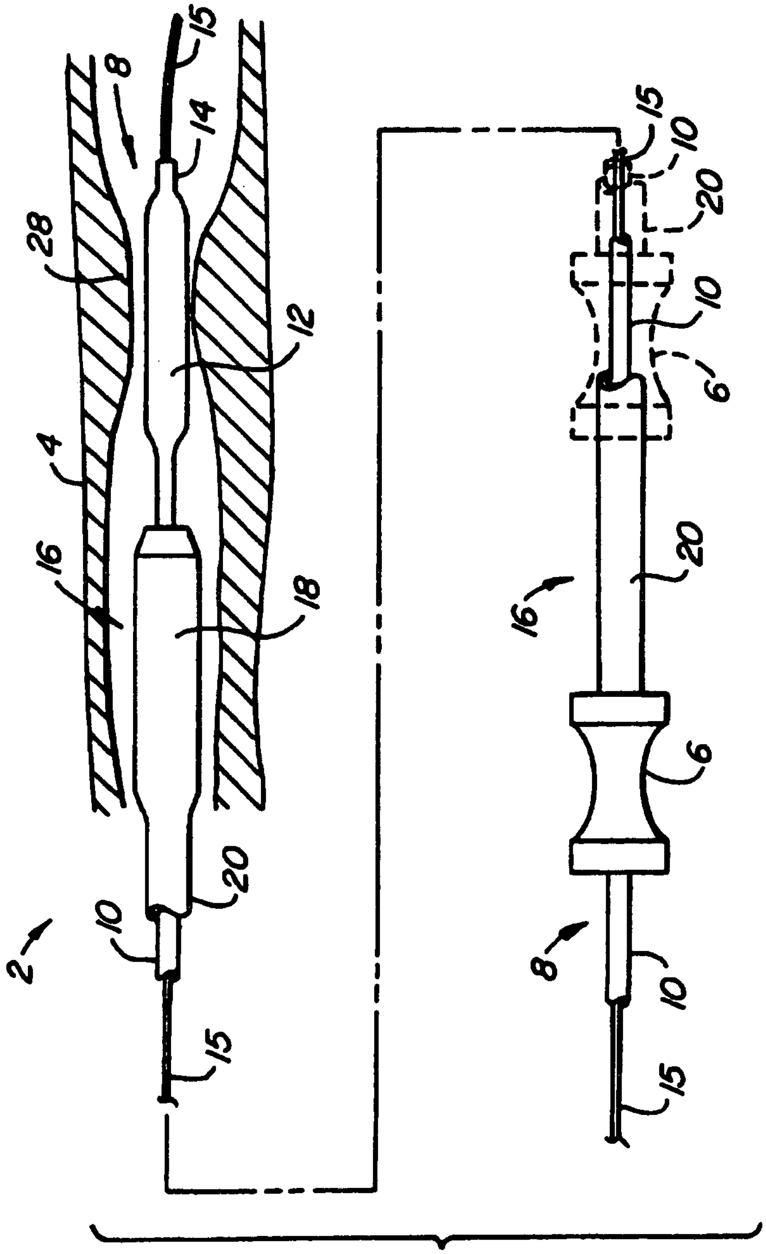

15
8
14
28
12
4
16
18
20
10
2
15
15
10
20
10
10
6
20
16
6
8
10
15

FIG. 1.

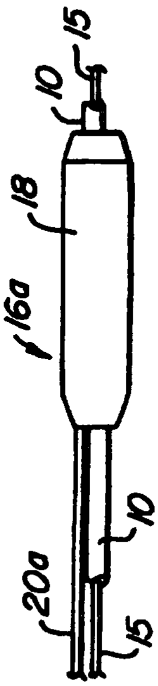

15
10
18
16a
10
20a
15

FIG. 4.

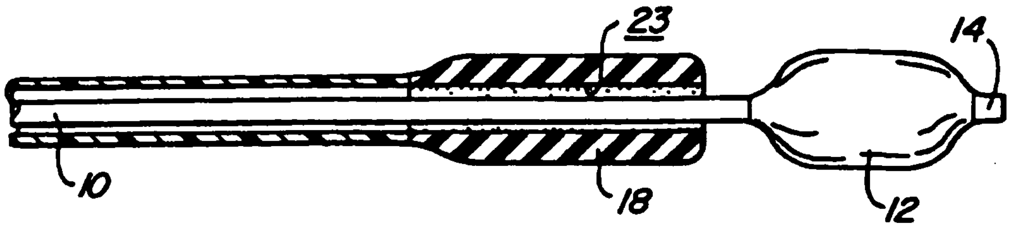


FIG. 1A.

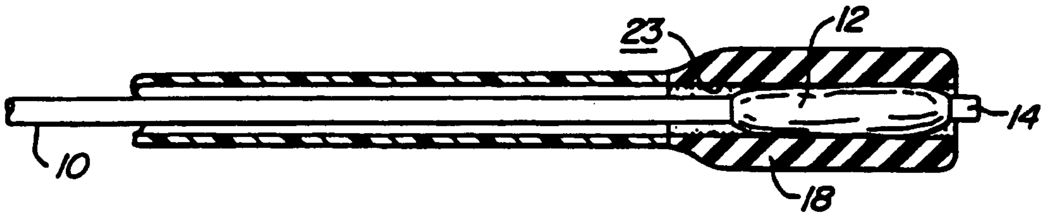


FIG. 1B.

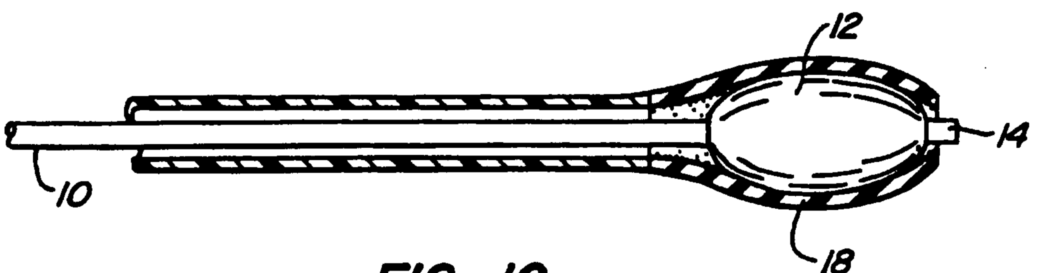


FIG. 1C.

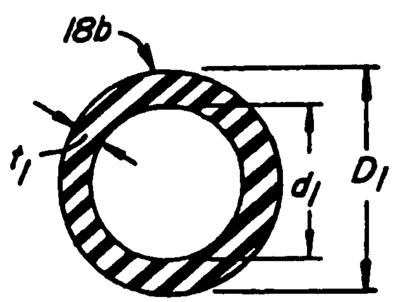


FIG. 3.

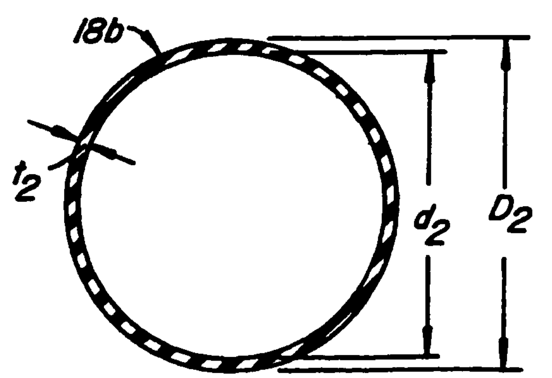


FIG. 3A.

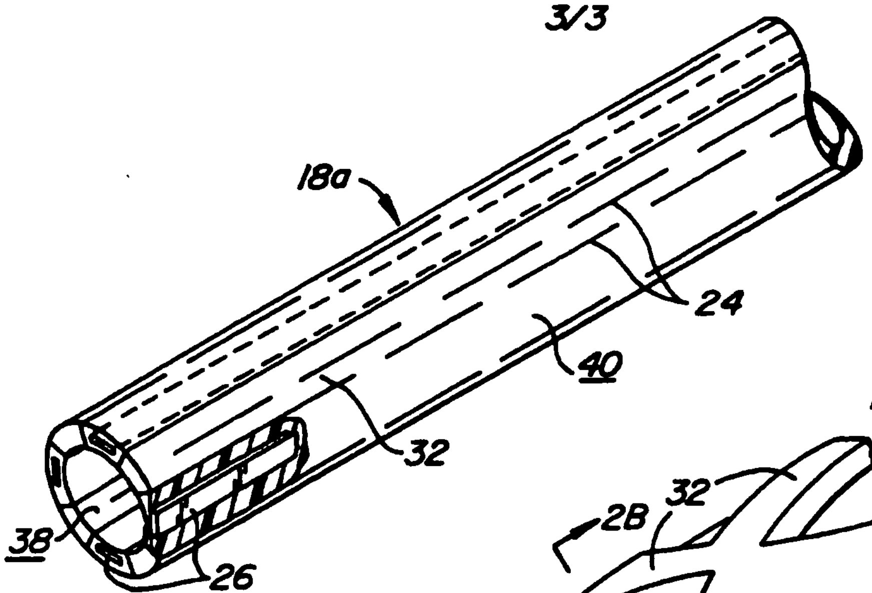


FIG. 2.

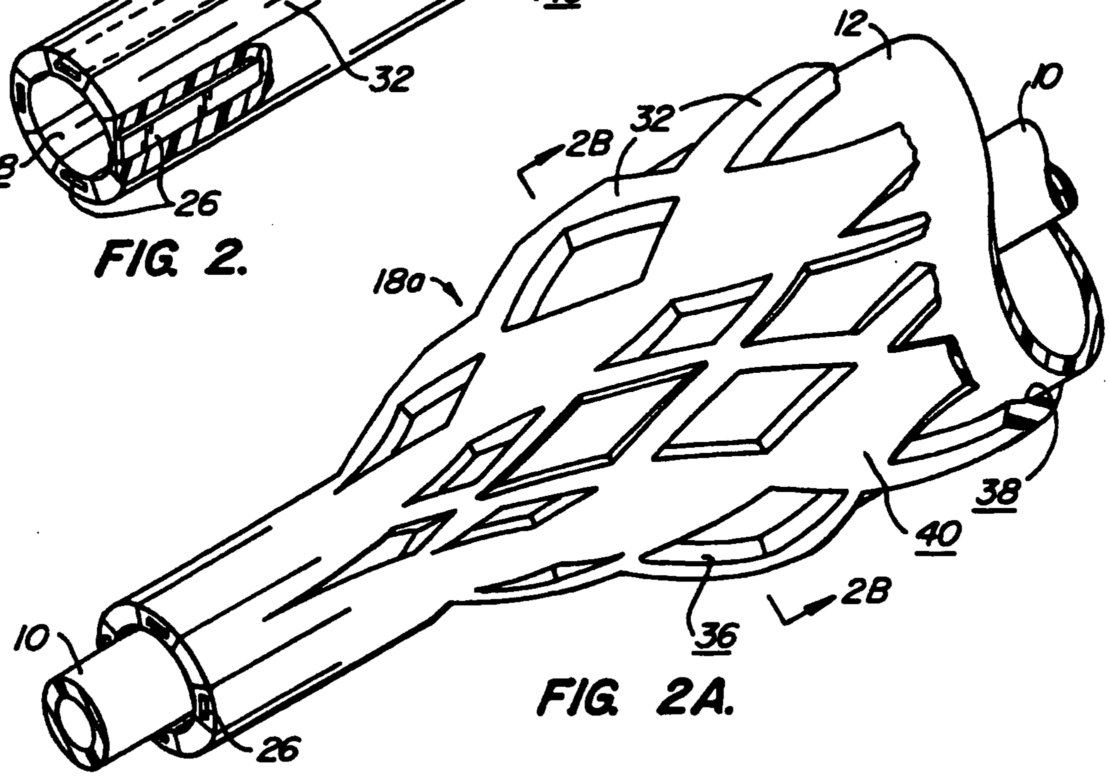


FIG. 2A.

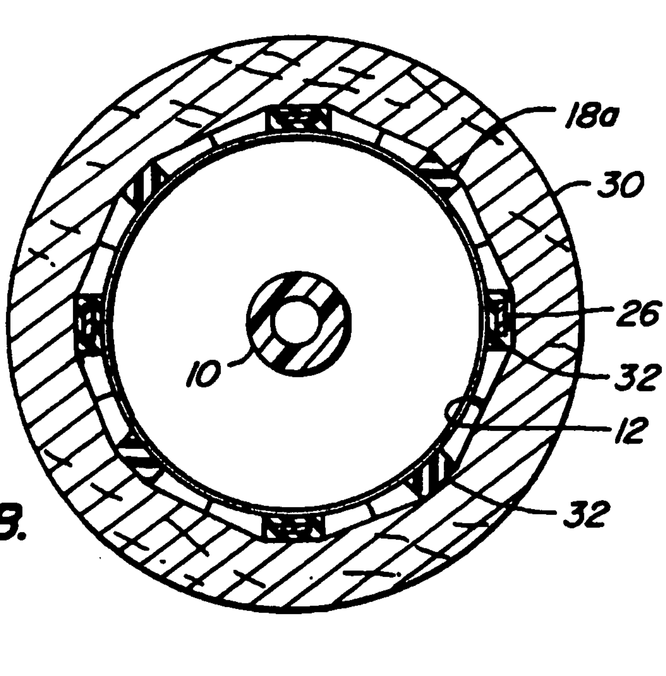


FIG. 2B.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US95/10099

A. CLASSIFICATION OF SUBJECT MATTER

IPC(6) :A61M 25/00
US CL :604/96
According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 604/53, 96, 101, 265; 606/192, 194

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

NONE

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

NONE

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US, A, 5,257,974 (COX) 02 November 1993, note Figs. 20, 27-29 and 30-32, and column 13 lines 59-64.	1-11, 14-22, 37, 38, 40-45, 49, 50, 52-57
A	US, A, 5,180,366 (WOODS) 19 January 1993, note Abstract.	23-36, 61-78
A, P	US, A, 5,364,356 (HOFLING) 15 November 1994, note Abstract.	23-36, 61-78
A	US, A, 5,336,178 (KAPLAN ET AL.) 09 August 1994, note Abstract.	23-36, 61-78

☐ Further documents are listed in the continuation of Box C. ☐ See patent family annex.

* Special categories of cited documents:

"A" document defining the general state of the art which is not considered to be part of particular relevance

"E" earlier document published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
21 SEPTEMBER 1995	08 NOV 1995

Name and mailing address of the ISA/US	Authorized officer
Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231	CORRINE MCDERMOTT
Facsimile No. (703) 305-3230	Telephone No. (703) 308-2111